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EXAMINER	
MITRA, RITA	

ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/561,834	NAKANO, SHIGERU	
	Examiner	Art Unit	
	Rita Mitra	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *1,8 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 December 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/9/2006, 12/22/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants' response to Restriction Requirement mailed May 17, 2007, filed June 12, 2007 is acknowledged. Applicants have elected with traverse Group II, claims 2-7. The traversal is on the ground(s) that when all of the claims drawn to the elected invention are allowable, the non-elected inventions should be considered for rejoinder. Additionally, no search burden has been shown, even if the invention includes claims, which are independent or distinct. This is not found persuasive because independence or distinctness and search burden are not criteria in determining whether a restriction is proper when said restriction is made under PCT Rules 13.1 and 13.2.

The requirement is still deemed proper and is therefore made FINAL.

Status of the Claims

Claims 1, 8 and 9 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention. Therefore, claims 2-7 are currently under consideration.

Specification Objections

The disclosure is objected to because of the following informalities:

1) The continuity data has not been entered at page 1, line 1 of the specification.

2) The title of the invention is objected to for using the word "novel." It should be noted that novelty is a determination of the office not an assertion by Applicants.

A correction is required.

The abstract of the disclosure is objected to because using the word "novel." It should be noted that novelty is a determination of the office not an assertion by Applicants. Correction is required. See MPEP § 608.01(b).

Claim Objections

Claim 2 is objected to because of the following informalities:

Claim 2 is objected to because it depends from a non-elected claim, and also for containing non-elected subject matter.

Appropriate correction is required.

Drawings

The amino acid sequence in Figure 3 requires a sequence identifier in the drawing or in the Brief Description thereof.

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2 and 3 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claimed product, as written, does not sufficiently distinguish over the naturally occurring product in living organisms, i.e., DNA of genus *Acetobacter* or *Gluconacetobacter*. In the absence of "the hand of man", the naturally occurring processes are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206, USPQ 193 (1980) and M.P.E.P. 2105. "A DNA" is a non-statutory subject matter. A correction to recite "An isolated and/or purified DNA" would overcome this rejection.

Claim Rejections - 35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2 and 4-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a DNA encoding a protein that is (A) a protein comprising the amino acid sequence shown in SEQ ID NO: 2; or (B) a protein comprising an amino acid sequence derived from the amino acid sequence of SEQ ID NO: 2 by substitution, deletion, insertion, addition, or inversion of one or several amino acids and having a growth-

promoting function. As drawn, the claim encompasses unknown DNA. Further, the nucleotide can also encode a protein that has a sequence shown in SEQ ID NO: 2 (meaning any sequence found within SEQ ID NO: 2), and that sequence can have substitutions, deletions, insertions, additions, or inversions, so long as the protein has growth promoting function. This claim encompasses a vast genus of polynucleotides that have no correlation between the structure of the encoded polypeptide and its function of growth promoting. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 1 and 2, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid and/or protein itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 U SPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGFs were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only SEQ ID NO: 1 and 2, but not the full breadth of the claims, meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant.

The specification does not provide a disclosure of any particular structure to function/activity relationship in any DNA encoding an amino acid sequence which comprises a deletion, substitution and/or addition of one or several amino, acids with respect to the amino acid sequence shown in SEQ ID NO: 1. The specification also lacks description with respect to what function, if any, is required for any DNA encoding an amino acid sequence which comprises a deletion, substitution and/or addition of one or several amino acids with respect to the amino acid sequence shown in SEQ ID NO: 1. Further, the specification fails to describe any identification of structural characteristics or properties of any DNA encoding an amino acid sequence which comprises a deletion, substitution and/or addition of one or several amino acids with respect to the amino acid sequence shown in SEQ ID NO: 1.

Given the lack of additional representatives of a genus of DNAs of either one of followings: (a) DNA encoding the amino acid sequence shown in SEQ ID NO: 1 and (b) any DNA encoding an amino acid sequence which comprises a deletion, substitution and/or addition of one or several amino acids with respect to the amino acid sequence shown in SEQ ID NO: 1, and having growth-promoting properties as encompassed by the claim, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Claims 2 and 4-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated DNA with the sequence of SEQ ID NO: 1, or encoding the protein

with the amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for the multitude of nucleic acids claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claim encompasses any DNA encoding a protein that is (A) a protein having an amino acid sequence shown in SEQ ID NO: 2; or (B) a protein consisting of an amino acid sequence comprising substitution, deletion, insertion, addition, or inversion of one or several amino acids in an amino acid sequence shown in SEQ ID NO: 2 and having a growth promoting function. As drawn, the claim encompasses unknown DNA. Further, the nucleotide can also encode a protein that has a sequence shown in SEQ ID NO: 2 (meaning any sequence found within SEQ ID NO: 2), and that sequence can have substitutions, deletions, insertions, additions, or inversions, so long as the protein has growth promoting function. The claim encompasses a vast genus of polypeptides that have no correlation between their structure and function. The specification does not disclose which portions of SEQ ID NO: 2 are necessary to provide the claimed function (i.e. growth promoting). Protein chemistry is probably one of the most unpredictable areas of biotechnology. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures

that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). Clearly, variants or fragments of SEQ ID NO: 2 that maintained the characteristics of the SEQ ID NO: 2 could not be predicted, and there is no way to predict what specific response would be elicited.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key Word is 'undue,' not 'experimentation.'" (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or

absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

Claim 2 is so broad as to encompass any DNA of either one of followings: (a) DNA encoding the amino acid sequence shown in SEQ ID NO: 2 and (b) any DNA encoding an amino acid sequence derived from the amino acid sequence of SEQ ID NO: 2 by substitution, deletion, insertion, addition or inversion of one or several amino acids, and having growth-promoting function. The claims rejected under this section of U.S.C. 112, first paragraph, do not place any structural limits on the "any DNA encoding an amino acid sequence which comprises a substitution, deletion, insertion, addition or inversion of one or several amino acids, and having growth-promoting function with respect to the amino acid sequence shown in SEQ ID NO: 2 ." Since the nucleic acids encoding a polypeptide determines its structural and functional properties, predictability of which nucleic acid sequence can be used while obtaining the desired function in the encoded protein requires a knowledge of and guidance with regard to which nucleic acids and amino acids of the polypeptide's sequence, if any, are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the nucleic acid sequence and its encoded polypeptide's structure relates to its desired function. In addition, the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of different DNA sequences and encoded polypeptides.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims,

and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any DNA encoding an amino acid sequence which comprises a substitution, deletion, insertion, addition or inversion of one or several amino acids, with respect to the amino acid sequence shown in SEQ ID NO: 2 because the specification does not establish: (A) regions of any DNA structure which may be modified without affecting the desired biological activity, i.e., the growth-promoting function; (B) the general tolerance of any DNA to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleic acid residue with an expectation of obtaining the desired biological function in the encoded polypeptide; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Because of this lack of guidance, and the fact that the relationship between the polynucleotide sequence and the encoded proteins' activity/function is not well understood and unpredictable (e.g., see Ngo et al. in "The Protein Folding Problem and Tertiary Structure Prediction," 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), it would require undue experimentation for one skilled in the art to make and use the claimed invention.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any

DNA encoding an amino acid sequence which comprises a substitution, deletion, insertion, addition or inversion of one or several amino acids, with respect to the amino acid sequence shown in SEQ ID NO: 2 while having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, i988).

Claim Rejections - 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is rendered indefinite by the phrase 'stringent condition' of hybridization. The specification at page 11 indicates the generic washing conditions after hybridization, however no specific 'stringent condition' for hybridization has been provided. This rejection can be overcome by including a desired specific 'stringent condition' in the claim. Claims 4-7 are ejected as depending from rejected claims 3.

Claim Rejections - 35 USC § I02

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by WPCOMMENT, Accession CP000009_19/c from *Gluconobacter oxydans* (see SEQ ID NO: 2 sequence alignment, result 2, database: GenEmbl).

The instant claim 3 is drawn to a DNA encoding a protein described in following (A), (B) or (C): (A) A DNA comprising nucleic acid sequence of nucleotides 180-1376 with respect to SEQ ID NO:1. (B) A DNA being capable of hybridizing to a DNA consisting of a sequence complementary to the nucleotide sequence of nucleotides 180-1376 with respect to SEQ ID NO:1 and encoding a protein having a growth-promoting function. (C) A DNA being capable of hybridizing to a DNA consisting of a nucleotide sequence produced from a part of the nucleotide sequence of nucleotides 180-1376 with respect to SEQ ID NO:1, having a function as a primer or a probe and encoding a protein having a growth-promoting function.

Accession CP000009_19/c from *Gluconobacter oxydans*, shows a DNA sequence that has 70.6% percent similarity, 60.9% best local similarity and 57% query match (see SEQ ID NO: 2 sequence alignment, result 2, database: GenEmbl), thus anticipating claim 3, which requires a DNA fragment of SEQ ID NO: 1 capable of hybridizing to a DNA consisting of a nucleotide sequence produced from a part of the said fragment with respect having a function as a primer or a probe and encoding a protein sequence of SEQ ID NO: 2 having a growth-promoting function.

Conclusion

No claim is allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita Mitra whose telephone number is (571) 272-0954. The examiner can normally be reached on M-F, 10:00 am to 7:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen K. Bragdon can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rita Mitra, Ph. D.

September 20, 2007

JON WEBER
SUPERVISORY PATENT EXAMINER